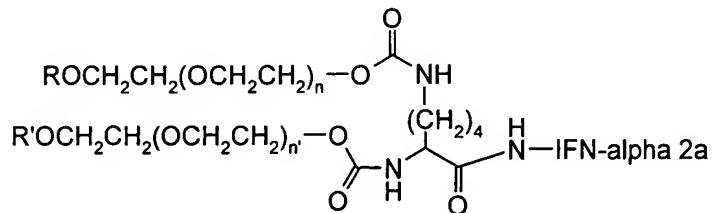


Claims

1. A positional isomers of pegylated interferon alpha 2a of the formula



wherein R and R' are independently lower alkyl; n and n' are integers having a sum of from 600 to 1500 and the bond to the IFN-alpha 2a is at a lysine residue selected from the group consisting of Lys(31) (PEG-Lys(31)), Lys(49) (PEG-Lys(49)), Lys(70) (PEG-Lys(70)), Lys(83) (PEG-Lys(83)), Lys(112) (PEG-Lys(112)), Lys(121) (PEG-Lys(121)), Lys(131) (PEG-Lys(131)), Lys(134) (PEG-Lys(134)) and Lys(164) (PEG-Lys(164)).

2. The positional isomers of pegylated interferon alpha 2a of claim 1 which is PEG-Lys(31).

3. The positional isomers of pegylated interferon alpha 2a of claim 1 which is PEG-Lys(134).

4. The positional isomers of pegylated interferon alpha 2a of claim 1, wherein the average molecular weight of the polyethylene glycol moiety (PEG moiety) in said pegylated interferon is about 40000 daltons.

5. The positional isomers of pegylated interferon alpha 2a of claim 2, wherein the average molecular weight of the polyethylene glycol moiety (PEG moiety) in said pegylated interferon is about 40000 daltons.

6. The positional isomers of pegylated interferon alpha 2a of claim3, wherein the average molecular weight of the polyethylene glycol moiety (PEG moiety) in said pegylated interferon is about 40000 daltons.

7. A method for the isolation of positional isomers of pegylated interferon alpha 2a, comprising
- a) separating the positional isomers on a preparative liquid chromatography column with a weak-cation exchange matrix; and
 - b) further separating and purifying the fractions from step a) on a preparative column with a strong-cation exchange matrix.
8. The method according to claim 7, wherein the chromatographic step a) is conducted by applying a linear pH gradient from about pH 3.8 to pH 8.0, of increasing sodium acetate concentration.
9. The method according to claims 7, wherein the chromatographic step b) is conducted with linear gradient of a sodium acetate buffer (A) to a potassium phosphate buffer (B) starting from an initial pH 4.2 to about 4.6 to a final pH of about pH 6.4 to about 6.8, said buffer solutions containing in addition up to 12% ethanol and up to 1.5% diethylene glycol.
10. The method according to claim 7, characterised that the chromatographic steps are carried out at a temperature of about 27° C to about 35° C, preferably at a temperature of about 30 to 32°C.
11. A pharmaceutical composition for the treatment or prophylaxis of viral or immunomodulatory diseases comprising a pharmacologically effective amount of a positional isomer of pegylated interferon alpha 2a according to claim 1 and a therapeutically inert carrier..
12. The pharmaceutical composition of claim 11 wherein the pegylated interferon alpha 2a is PEG-Lys(31).
13. The pharmaceutical composition of claim 11 wherein the pegylated interferon alpha 2a is PEG-Lys(134).